REMARKS

This Response is submitted in reply to the final Office Action mailed on June 15, 2010. A Petition for a three month extension of time and a Request for Continued Examination ("RCE") are submitted herewith this Response. The Director is authorized to charge $1,110.00 for the Petition for a two month extension of time, $810.00 for the RCE, and any additional fees that may be required, or to credit any overpayment to Deposit Account No. 02-1818. If such a withdrawal is made, please indicate the Attorney Docket No. 3712036-00701 on the account statement.

Claims 1 and 5-21 are pending in this application. Claims 2-4 were previously canceled without prejudice or disclaimer. In the Office Action, Claims 1 and 5-21 are rejected under 35 U.S.C. §103. For at least the reasons set forth below, Applicants respectfully traverse the rejections and request that the rejections be reconsidered and withdrawn.

In the Office Action, Claims 1, 5, 6, 9 and 14-16 are rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,306,908 to Carlson et al. ("*Carlson*") in view of U.S. Patent No. 5,902,578 to Halpin-Dohnalek et al. ("*Halpin-Dohnalek*") as evidenced by Bifidobacterial NPL and DHA NPL. Claim 7 is rejected under 35 U.S.C. §103(a) as being unpatentable over *Carlson* in view of *Halpin-Dohnalek* and further in view of Effect of Bifidobacterium longum BB536 yogurt administration on the intestinal environment of healthy adults by T. Ogata et al. ("*Ogata*") as evidence by Bifidobacterial NPL. Claim 8 is rejected under 35 U.S.C. §103(a) as being unpatentable over *Carlson* in view of *Halpin-Dohnalek* and further in view of EP 0904784 to Van Hoey-De-Boer et al. ("*Van Hoey-De-Boer*") as evidenced by Bifidobacterial NPL. Claim 10 is rejected under 35 U.S.C. §103(a) as being unpatentable over *Carlson* in view of *Halpin-Dohnalek* and further in view of *Van Hoey-De-Boer* and *Ogata* as evidenced by Bifidobacterial NPL. Claims 11-13 and 17-21 rejected under 35 U.S.C. §103(a) as being unpatentable over *Carlson* in view of *Halpin-Dohnalek* and further in view of U.S. Patent No. 6,777,391 to Kratky et al. ("*Kratky*") as evidence by Threonine NPL and Bifidobacterial NPL. For at least the reasons set forth below, Applicants respectfully submit that the cited references are deficient with respect to the present claims.

Independent Claim 1 recites, in part, infant or follow-on formulas comprising a source of lipids comprising ARA and DHA, wherein the DHA content is between 0.2 and 0.5% of the total

fatty acids in the lipid source. Independent Claims 14 and 16-17 recite, in part, methods comprising administering to an infant an infant or follow-on formula comprising a source of lipids comprising ARA and DHA, wherein the DHA content is between 0.2 and 0.5% of the total fatty acids in the lipid source.

Applicants have surprisingly found that feeding infants the formula of the present invention generally results in the promotion of the immune defenses of the infant, as has been demonstrated by an enhanced response to vaccinations and/or improved gut barrier function and lower levels of intolerance of cows' milk protein coupled with satisfactory physical development. These results are summarized in Examples 1 and 2 of the specification where infants that were fed a formula of the present invention were compared to infants that were fed a similar formula but without probiotics. The results demonstrate that infants fed the formulas of the present claims generally display strengthened immune defenses as demonstrated by an enhanced response to vaccinations and/or improved gut barrier function and lower levels of intolerance of cows' milk protein coupled with satisfactory physical development when compared with the control group. See, specification (US 2007/0031537), Examples at paragraphs [0069] – [0077].

Applicants previously submitted the methodology and trials for certain *in vitro* testing of certain exemplary compositions of the presently claimed invention. The methodology and trials detailed *in vitro* testing of compositions including ARA, DHA and *Lactobacillus paracasei* NCC 2461 (ST11). While *Lactobacillus paracasei* was selected for the present *in vitro* studies, Applicants submit that the presently claimed subject matter should not be limited to this probiotic. Generally, in the *in vitro* study, T84 cells were incubated overnight in serum free DMEM/F12 followed by a two hour pre-incubation with ST11 cells in the presence or absence of DHA/ARA. After the two hour pre-incubation, *Clostridium difficile* toxin A was added to the apical chamber. After an overnight incubation, transepithelial electrical resistances (TEER) were measured, and the protection of ingredients, alone and in combination, were measured. The results of the test indicate that a combination of a probiotic and DHA/ARA provides better results than either ingredient alone. Applicants respectfully submit that the cited references fail to disclose each and every element of the present claims. Applicants further submit that the

skilled artisan would have no reason to combine the cited references because the cited references teach away from each other and the present claims.

Regarding each of independent Claims 1, 14, 16 and 17, *Carlson*, *Halpin-Dohnalek* and *Kratky* all fail to disclose or suggest infant or follow-on formulas comprising a source of lipid comprising ARA and DHA, wherein the DHA content is between 0.2 and 0.5% of the total fatty acids in the lipid source as is required, in part, by the present claims. The Patent Office cites *Carlson* as teaching DHA. See, Office Action, pages 3-4. However, the Patent Office also states that "[a]though Carlson fails to explicitly teach arachidonic acid and docosahexaenoic acid both being present in the formula wherein the docosahexaenoic acid amount is 0.2-0.5%, *Carlton* does teach that the amount of docosahexaenoic acid may range from 0.25-35 mg…[i]n light of these teachings, one of ordinary skill in the art would have found it obvious to slightly increase the docosahexaenoic acid content to 7 mg…to a slightly higher amount in order to boost the brain health boosting properties (produce known effects) of the formula (see docosahexaenoic acid NPL). Also, in light of the teachings discussed previously, the claimed range would have been discoverable by routine experimentation by one of ordinary skill in the art seeking to boost the brain health enhancing properties of the 'formula'." See, Office Action, page 3, lines 10-20. Applicants respectfully disagree.

Besides failing to disclose or suggest the range of DHA content in the total fatty acids as claimed, *Carlson* does not even mention any percentages or the requirement of specific percentages of any specific fatty acids (e.g., ARA and DHA) in the total fatty acids in the lipid source as is required, in part, by the present claims. Indeed, even if *Carlton* discloses one embodiment of a fatty acid profile having ARA and DHA, it is not proper for the Patent Office to extrapolate weight percents of ARA and DHA in different embodiments since total weight percents change based on the compositions in the lipid profile.

Further, rather than relating the compositions to the promotion of the immune system, *Carlson* relates to compositions for reducing the incidence of necrotising enterocolitis, which is a life-threatening condition that is generally only a risk factor for infants born prematurely. To address this, *Carlson* teaches administering ARA and DHA, preferably in the form of phospholipids, as these are believed to be more effective than the triglyceride form. See, *Carlson*, column 2, lines 33-39 and column 2, lines 20-45.

Halpin-Dohnalek and *Kratky* each fail to remedy the deficiencies of *Carlson*. For example, the Patent Office cites *Halpin-Dohnalek* for disclosing probiotics for use in an infant formula. See, Office Action, page 3, line 21-page 4, line 9. Moreover, the Patent Office cites *Kratky* for disclosing modified sweet whey proteins with no CGMP or reduced CGMP. See, Office Action, page 7, line 17-page 8, line 18. As such, these secondary references fail to remedy the deficiencies of *Carlson*. Specifically, the secondary references fail to disclose or suggest infant or follow-on formulas comprising a source of lipid comprising ARA and DHA, wherein the DHA content is between 0.2 and 0.5% of the total fatty acids in the lipid source as is required, in part, by each of the independent Claims 1, 14, 16 and 17.

Additional secondary references *Ogata* and *Van Hoey-De-Boer* are cited in the Office Action for disclosing elements of dependent claims. The Patent Office cites *Ogata* for disclosing Bifidobacterium longum BB536 recited in Claim 7. See, Office Action, page 5, line 17-page 6, line 2. Furthermore, the Patent Office cites *Van Hoey-De-Boer* for disclosing lactobacillus rhamnosus GG recited in Claim 8. See, Office Action, page 6, lines 9-18. Like secondary references *Halpin-Dohnalek* and *Kratky*, neither *Ogata* nor *Van Hoey-De-Boer* discloses or even suggests infant or follow-on formulas comprising ARA and DHA, wherein the DHA content is between 0.2 and 0.5% of total fatty acids in the lipid source as is required, in part, by independent Claims 1, 14, 16 and 17. Accordingly, *Halpin-Dohnalek*, *Ogata*, *Van Hoey-De-Boer* and *Kratky* all fail to remedy the deficiencies of *Carlson*.

The Patent Office asserts that the secondary references were cited solely for specific elements of dependent claims. See, Office Action, pages 11-14. As such, it is clear that the secondary references fail to remedy the deficiencies of *Carlson*. Applicants submit, however, that if each individual reference fails to disclose or suggest the same element of the present claims, then the references alone, or in combination, are deficient with respect to the present claims. Here, each reference cited fails to disclose or suggest infant or follow-on formulas comprising a source of lipid comprising ARA and DHA, wherein the DHA content is between 0.2 and 0.5% of the total fatty acids in the lipid source as is required, in part, by the present claims. Therefore, the combination of references is deficient.

Applicants also respectfully submit that the skilled artisan would have no reason to combine the cited references because the cited references teach away from the present claims and

from each other. For example, and as discussed above, *Carlson* is entirely directed to enteral formulas for reducing the incidence of necrotising enterocolitis, a life-threatening condition that is generally only a risk factor for infants born prematurely. The enteral formulas contain long-chain polyunsaturated fatty acids (PUFAs), e.g., arachidonic acid (AA) and docosahexaenoic acid (DHA). See, *Carlson*, Abstract.

Halpin-Dohnalek is entirely directed toward the use of a mixture of three different probiotic bacterial species including a *Lactobacillus reuteri*, a *Lactobacillus acidophilus* and a *Bifidobacterium infantis* to prevent infectious diarrhea. See, *Halpin-Dohnalek*, Abstract. *Halpin-Dohnalek* teaches that the presence of all three of these strains is necessary to achieve the desired result. See, *Halpin-Dohnalek*, column 4, lines 57-60. Although mention is made of infant formula, the treatment is primarily directed to older children, as may be seen from the clinical study described at Example II. In fact, these probiotics would not be suitable for infants since both *Lactobacillus reuteri* and *Lactobacillus acidophilus* produce D(-) lactic acid and their consumption by children under three, particularly infants, is not recommended by the World Health Organization. Further, as stated above, *Halpin-Dohnalek* fails to even mention the promotion of the immune system of infants.

In regards to the asserted combination of *Carlson* with *Halpin-Dohnalek*, Applicants previously submitted an article by Kankaanpää, which demonstrates that the skilled artisan would be deterred from combining probiotics and polyunsaturated fatty acids (PUFAs), as is required, in part, by the present claims. Specifically, Kankaanpää states that "[a]s polyunsaturated fatty acids (PUFA) possess antimicrobial properties, they may deter the action of probiotics" (emphasis added). See, Kankaanpää, Abstract. Kankaanpää also states that "physiologically relevant levels of free PUFA may influence the functions of probiotics. Consequently, non-adhered probiotics may be washed out from the gastrointestinal tract and potential health benefits may be compromised" (emphasis added). See, Kankaanpää, page 153. Applicants respectfully submit, therefore, that the Kankaanpää reference would have discouraged the skilled artisan from combining probiotics and PUFA to arrive at the present claims. Therefore, the skilled artisan would have no reason to combine at least *Carlson* with *Halpin-Dohnalek* in view of the Kankaanpää reference.

The Patent Office asserts that "[t]he Kankaanpää reference does not appear to establish that combining probiotics with PUFA's would be disadvantageous in the references cited by [the] examiner." See, Office Action, page 13, lines 18-19. Applicants submit that although the Kankaanpää reference may not compare specific compositions recited in the cited references, Kankaanpää does teach the skilled artisan that compositions having PUFA's and probiotics may not be beneficial in combination in compositions.

Regarding the remaining secondary references, *Ogata* is entirely directed toward the effects of *Bifidobacterium longum* BB536 yogurt on the intestinal environment of healthy adults. See, *Ogata*, Abstract. Although *Ogata* mentions the use of *Bifidobacterium longum* BB536, the article is entirely directed toward consumption by healthy adults and fails to even mention administration of BB536 to infants to strengthen their immune systems. As a result, *Ogata* would not even be considered by one skilled in the art that is seeking to improve the immune system of infants.

Van Hoey-De-Boer is entirely related to a nutritional composition containing a minimum of three different probiotic strains with the intention of providing protection against infection all the way along the gastro-intestinal tract, thus obviating the need to identify the type of micro-organism responsible for the infection. See, *Van Hoey-De-Boer,* Abstract. The benefits of such compositions include, for example, therapy or prophylaxis of multiple disorders of the gastrointestinal tract such as IBS, Crohn's disease and cancer of the GI tract. However, *Van Hoey-De-Boer* fails to even suggest that probiotics may play a useful role in strengthening the immune system of infants as claimed.

Kratky is entirely directed toward an infant formula having a low threonine content and whey protein. See, *Kratky*, column 1, lines 4-25. *Kratky* fails to disclose any polyunsaturated fatty acids, including ARA and DHA, or any probiotics. Further, *Kratky* fails to disclose or even suggest strengthening the immune system of infants.

As such, the compositions and methods of the cited references are directed toward completely unrelated products having completely unrelated objectives. Accordingly, the skilled artisan would have no reason to combine the cited references to arrive at the present claims. Indeed, the skilled artisan would not arrive at the present claims by reviewing such cited references having widely varying applications and entirely different objectives. Further, if the

proposed modification would render the prior art invention being modified unsatisfactory for its intended purpose, then there exists no reason for the skilled artisan to make the proposed modification. *In re Gordon*, 733 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984).

The Patent Office asserts, however, that one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See, Office Action, page 1, lines 1-6. As discussed above, however, if each individual reference fails to disclose or suggest the same element of the present claims, then the references alone, or in combination, are deficient with respect to the present claims. Here, each reference cited fails to disclose or suggest infant or follow-on formulas comprising a source of lipid comprising ARA and DHA, wherein the DHA content is between 0.2 and 0.5% of the total fatty acids in the lipid source as is required, in part, by the present claims. Therefore, the combination of references is deficient.

Applicants also respectfully submit that the Patent Office has applied hindsight reasoning by attempting to selectively piece together teachings of each of the references in an attempt to recreate what the claimed invention discloses. The Patent Office asserts, however, that as long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See, Office Action, page 14, lines 7-14. However, as evidenced by the Kankaanpää reference, the knowledge that was within the level of ordinary skill would at the time of the claimed invention establishes that the skilled artisan would be discouraged from combining probiotics and PUFAs, such as ARA and DHA, to arrive at the present claims. With that knowledge, it is clear that the Patent Office applied hindsight reasoning by gleaning knowledge from Applicants' disclosure over that which was known at the time of the claimed invention (e.g., the Kankaanpää reference).

Applicants also submit that if it were proper for the Patent Office to combine any number of references to arrive at the present claims simply because each reference suggests an element of the present claims, then every invention would effectively be rendered obvious. Instead, the skilled artisan must have a reason to combine the cited references to arrive at the present claims. Applicants respectfully submit that such a reason is not present in the instant case.

Accordingly, Applicants respectfully request that the obviousness rejections with respect to Claims 1 and 5-21 be reconsidered and the rejections be withdrawn.

For the foregoing reasons, Applicants respectfully request reconsideration of the above-identified patent application and earnestly solicit an early allowance of same. In the event there remains any impediment to allowance of the claims which could be clarified in a telephonic interview, the Examiner is respectfully requested to initiate such an interview with the undersigned.

Respectfully submitted,

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